REMARKS

Claims 1-3, 5-10, 88-92 are now pending in the application.

1. Claim Amendments

Applicants have amended claims 1-3, and 6-9. Support for the amendments can be found in the original claims and in the specification, for example, at page 19 lines 10-30 and at page 16, line 21 to page 17, line 10. New claims 91 and 92 have been added. Support for these claims can be found in original claims 1 and 8. Claims 4, 30-34 and 83-87 have been cancelled. Cancellations and amendments are made without prejudice for filing a continuation, divisional or continuation-in-part application directed to the cancelled subject matter.

2. Claim rejections under 35 U.S.C. § 112

The Examiner has indicated that claims 1-7, 30-34, 83, 84 and 86 stand rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for astragaloside IV, cycloastragenol, astragenol, astragaloside IV-16-one, cycloastragenol 6-beta-D-glucopyranoside and cyclsoastragenol-3-beta-D-xylopyranoside, does not reasonably provide enablement for the compound of formula I as encompassed by the claims. In particular, the Office Action states that the term "glycoside" is not limited to any specific structural formula of a saccharide and encompasses all monosaccharides etc.

Applicants have amended Claim 1 to recite that X^1 is hydroxy or β-D-xylopyranoside, X^2 is hydroxy or β-D-glucopyranoside and X^3 is hydroxy or keto. Accordingly, the type of glycoside has now been identified in the claim. Applicants have canceled claims 4, 30-34 and 83, 84 and 86.

The claimed invention is now fully enabled. One skilled in the art, given the disclosure of the specification would be able to make and use the claimed invention. Methods of making the claimed compounds are set forth in the Examples in the specification from pages 39-50. Methods of testing the claimed compounds are set forth in the specification at pages 24 – 30.

For these reasons, withdrawal of this rejection is respectfully requested.

3. Claim Rejections under 35 U.S.C. § 102(a)

Claims 30-34 and 83-87 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Binder (US Patent No. 5,770,578) or Kitigawa et al. (Chem. Pharm. Bull. 31(2), 689-697 (1983)). Each of Binder et al., and Kitigawa et al. allegedly discloses the claimed compositions comprising astragaloside and/or astragenol compounds.

Applicants have canceled claims 30-34 and 83-87 without prejudice to filing a continuation application directed to the canceled subject matter.

This rejection is rendered moot and withdrawal of this rejection is respectfully requested.

4. Claim Rejections under 35 U.S.C. § 103

I. Claims 1-10 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Binder (US Patent No. 5,770,578) in view of Bodhar et al., (Science vol. 279, January 1998).

The Office Action states that Binder discloses contacting a cell or tissue with astragaloside but does not disclose identifying a cell or tissue in which an increase in telomerase activity is desired. Bodnar et al. allegedly teach that normal human cells undergo a finite number of cell divisions which has an implication in aging and age-related pathologies. Therefore, the Office Action states that Bodnar suggests that all animals are in need of cells or tissue having increase telomerase activity since all animals face aging. Since administration of astragaloside disclosed by Binder et al. would allegedly inherently result in increased telomerase activity and since telomerase activity is generally desired, the claimed methods are deemed *prima facie* obvious over the cited art.

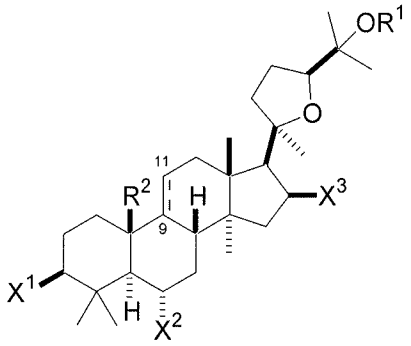
Applicants disagree for the following reasons.

Applicants submit that the Examiner has failed to apply the proper legal standard for comparing the present invention to the cited references. In *KSR International Co. v. Teleflex Inc.* 127 S. Ct. 1727 (2007), the Supreme Court affirmed the requisite inquiry for determining obviousness originally set forth in *Graham v. John Deere Co. of Kansas City* 383 U.S. 1 (1966) and noted that the teaching, suggestion, motivation test subsequently formulated by Court of Customs and Patent Appeals and followed by Court of Appeals for the Federal Circuit provided useful insight in determining obviousness, although the test should not be applied in a rigid manner. Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the Graham analysis" KSR 127 S.Ct. at 1731. The Court specifically acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. Moreover, the Federal Circuit has cautioned "to the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these 'identified, predictable solutions' may present a difficult hurdle because potential solutions are less likely to be genuinely predictable." *Eisai Co. v. Dr Reddy's Laboratories* 533 F3rd 1353 (Fed. Cir. 2008).

MPEP § 2143 provides guidance for establishing a prima facie case of obviousness, noting that there are three elements to establishing a prima facie case. The elements include some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. The references should provide a reasonable expectation of success that the suggested combination may be achieved. Finally, the prior art reference (or references combined) should teach or suggest all the claim limitations. The Patent and Trademark Office (PTO) bears the burden of initially establishing a *prima facie* case of obviousness. MPEP § 2142. The Office has not met its burden in the instant case.

Applicant has amended the current claims. The claimed invention is now directed to a method of increasing telomerase activity in a cell or tissue, comprising

identifying a cell or tissue in which an increase in telomerase activity is desired, and contacting said cell or tissue with a formulation of an effective amount of an isolated compound of formula **I**:



where:

X^1 is hydroxy or β-D-xylopyranoside; X^2 is hydroxy or β-D-glucopyranoside; X^3 is hydroxy or keto;

OR' is hydroxy; and R^2 is methyl and ---- represents a double bond between carbons 9 and 11; or, R^2 forms, together with carbon 9, a fused cyclopropyl ring, and ---- represents a single bond between carbons 9 and 11 wherein telomerase activity is increased. Claim 1 includes the step of identifying cells or tissues in which an increase in telomerase activity is desired.

Binder teaches that the administration of astragaloside (ASIV) to human umbilical vein endothelial cells (HUVECs) resulted in a dose dependent increase of tPA mRNA and antigens and a decrease in the PAI-1 mRNA and antigen in the cells. (Examples 7 and 8) Binder also teaches that administration of ASIV simultaneously with LPS to HUVECs reduced the upregulation of the PAI-1 antigen by the LPS. (Example 9) The Examiner agrees that Binder does not teach or suggest that astragaloside IV or the other compounds of the present invention would be useful for increasing the activity of telomerase in a cell. One skilled in the art would not know or be motivated by Binder to use the compounds of the present invention to increase the telomerase activity in a tissue or cell.

Bodnar *et al.*, teaches that the some cells lines such as retinal pigment epithelial cells and foreskin fibroblasts do not express telomerase. (Page 349 abstract and middle column). Bodnar et al teaches that transfection of such cells with vectors encoding the human telomerase catalytic subunit results in expression of telomerase and elongated telomeres. Bodnar *et al.*, does not teach or suggest that astragaloside IV or the other compounds of the present invention would be useful for increasing the activity of telomerase in a cell.

As the courts have held, there must be some teaching or suggestion in the cited art to carry out the claimed invention.

The present application is directed to the discovery that certain isolated compounds can be used to increase the telomerase activity of cells. Neither Binder nor Bodnar teach or suggest that the administration of astragaloside IV or the other claimed compounds will increase telomerase activity. Accordingly, one skilled in the art would not be taught or motivated to administer the claimed compound for increasing telomerase activity. Absent such teaching or motivation the claimed methods are not obvious.

The Examiner states that administration of astragaloside IV as disclosed by Binder et al. would inherently result in increased telomerase activity and since telomerase activity is generally desired (by the teachings of Bodhar *et al.*), the claimed methods are deemed *prima facie* obvious.

A claim limitation is inherent in the prior art if it is necessarily present in the prior art, not merely probably or possibly present. *Akamai Technologies v. Cable & Wireless Internet Services, Inc* 344 F.3d 1186, 68 USPQ 2d 1186.

Bodnar *et al.* teaches that telomere loss is thought to control entry into senescence. Human telomere repeats are synthesized by telomerase. "Telomerase is active in germline cells and in humans, telomeres in these cells are maintained at about 15 kilobase pairs (kbp). In contrast, telomerase is not expressed in most human somatic tissues and telomere length is significantly shorter. The telomere hypothesis of cellular aging proposes that cells become senescent when progressive telomere

shortening during each cell division produces a threshold telomere length." (emphasis added) (page 349, col. 1-2).

Therefore, contrary to the Examiner's statement, it is not necessarily follow from Binder et al., and Bodnar et al. that telomerase activity could be increased in all somatic cells, since Bodnar teaches that not all cells express telomerase. Accordingly, the combination of Binder and Bodnar does not teach the administration of astragaloside IV or the other claimed compounds for the purpose of increasing telomerase activity in cells. Furthermore, one of skill in the art, would not have a reasonable expectation that the administration of the claimed compounds would increase telomerase activity. Accordingly, the current claims are not inherently in the prior art. For these reasons, withdrawal of this rejection under 35 U.S.C. 103(a) is respectfully requested.

II. Claims 88-90 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Binder (US Patent No. 5,770,578) in view of Bodnar et al. as applied to claims 1-10 above and further in view of Kitigawa et al. (Chem. Pharm. Bull. 31(2), 689-697 (1983)).

Kitigawa et al. allegedly disclosed the related astragaloside and astragenol compounds extracted from *Astragali Radix*, a known Chinese medicine. It would have been allegedly obvious to substitute various astragaloside and astragenol compounds in the method discussed by Binder et al., because a person would have expected the closely structurally related compounds to have similar activity.

This rejection is traversed for the following reasons. Binder and Bodhar have already been discussed. Binder only teaches the administration of astragaloside IV to HUVEc cells to increase tPA antigen and decrease PAI-1 antigen. Binder does not teach administration astragaloside IV for increasing telomerase activity. Bodnar teaches the transfection of cells with the telomerase gene to increase telomerase expression. Bodnar does not teach the administration of small molecules to increase telomerase expression. Accordingly, neither Binder nor Bodhar teach or suggest that astragaloside IV or any of the claimed compounds would be useful to increase telomerase activity.

Kitigawa et al., allegedly teaches that astragenol and cycloastragenol can be generated by acid hydrolysis of Astragalus root. Kitigawa does not teach or suggest that astragaloside IV or any of the claimed compounds can be used to increase telomerase activity. Ktigawa does not teach or suggest that these compounds share any similar activities. Accordingly, the combination of Binder, Bodhar and Kitigawa does not teach a method of increasing telomerase activity by administration of the claimed compounds. Furthermore, the combination of Binder, Bodnar and Kitigawa does not give one of skill a reasonable expectation that administration of the compounds would increase telomerase activity. Accordingly, the combination of Binder, Bodnar and Kitigawa does not render the claimed invention obvious.

For these reasons, Applicants respectfully request that the rejections under 35 U.S.C. §103(a) be withdrawn.

IV. Conclusion

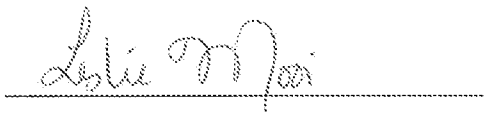
In view of the foregoing, the applicant submits that the claims now pending are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If the Examiner believes that a telephonic interview would expedite prosecution, the Examiner is encouraged to contact the undersigned.

No fees are believed due with this communication. However, the

Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 07-1139.

Respectfully submitted,



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